

REMARKS

Status of the Claims

Pending claims

Claims 1 to 9, 13, 14, and 17 to 45 are pending.

Advisory Action of May 20, 2003

As noted in the Advisory Action of May 20, 2003 (hereinafter "the Advisory Action"), Applicants' after final amendment of April 17, 2003, was not entered. Thus, as the instant amendment to the claims is being submitted in accordance with the Revised Amendment Practice under 37 CFR 1.121, Final Rule, dated June 30, 2003, effective July 30, 2003, the claim markings in the instant response show changes relative to the last entered amendment of August 09, 2002.

Claims amended, canceled and added in the instant amendment

In the present response, claims 26, 31 to 33, 35 and 38 to 44 are canceled, without prejudice; claims 1 to 3, 5 to 8, 13, 14, 19, 21, 24 to 30, 34, 36, 37 and 42 to 45 are amended; and new claims 46 to 67 are added. Thus, after entry of the instant amendment, claims 1 to 9, 13, 14, 17 to 25, 27 to 30, 34, 36, 37, and 42 to 67 are pending and under examination.

Both before and after the above changes and cancellations, and the addition of new claims, the invention was described in full, clear, concise, and exact terms and met all conditions for patentability under 35 USC 101 *et seq.* The scope of the claims of any resulting patent (and any and all limitations in any of said claims) shall not under any circumstances be limited to their literal terms, but are intended to embrace all equivalents.

Outstanding Rejections

Claims 1 to 9, 13, 14, and 17 to 45 are rejected under 35 U.S.C. §112, second paragraph. Claims 24, 25, and 27-45 are rejected under 35 U.S.C. §112, first paragraph. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Request for Substitution of Sequence Listing based upon Deposit

Applicants request substitution of the sequence listing on file with the sequence listing submitted herewith. Upon re-sequencing the plasmid, 18GC, identified in the instant application (SEQ ID NO:3 and SEQ ID NO:4) on, inter alia, page 4, lines 20-22, of the specification as originally filed and Figures 1A-1C, Applicants have noted three nucleotide discrepancies which did not result in any amino acid change in the amino acid sequence, SEQ ID NO:4, as originally filed. Accordingly, Applicants note that the changes to the substitute sequence listing does not affect the instant claims as amended.

Applicants have deposited the plasmid identified in the application with the ATCC on September 10, 2002. The deposit has been accepted and designated PTA-4654. Applicants, in the instant Response, seek to incorporate the correct sequence into the application with the ATCC deposit, the substitute sequence listing based upon the deposit, amended specification, amended drawings, and declarations. A copy of the papers to accept the sequence of the ATCC deposited organism, filed on December 12, 2002, in a related application, U.S. Application No. 09/886,400, was submitted in Applicants' response and amendment of April 17, 2003. Examination of the proper sequences is respectfully requested.

Drawings

Please enter substitute Figure 1, as submitted in Applicants' response and amendment of April 17, 2003, and replace the originally submitted drawing with the formal drawing enclosed herein. The amendment (change in the drawing) is based upon the sequence of *Thermococcus alcaliphilus* AEDII12RA α -galactosidase, 18GC, deposited with the ATCC located at 10801 University Blvd., Manassas, VA 20110-2209, on September 10, 2002, and designated as PTA-4654. Accordingly, Applicants submit that no new matter is introduced by the instant amendment.

Information Disclosure Statement

Applicants thank the Examiner for expressly considering (and initialing) the supplementary Information Disclosure Statement (IDS) and Form PTO-1449 submitted on October 10, 2002.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to hybridization wash conditions and stringent hybridization conditions can be found, inter alia, on page 6, lines 2 to 1. Support for claims directed to nucleic acids described by a percent sequence identity to an exemplary nucleic acid can be found, inter alia, on page 6, lines 12 to 21, and, page 9, second full paragraph. Support for claims directed to nucleic acids encoding polypeptides with alpha galactosidase activity comprising hydrolysis of raffinose, stachyose and verbascose can be found, inter alia, on page 2, lines 6 to 8. Support for claims directed to nucleic acids comprising a portion at least 12 contiguous nucleotides of a sequence of the invention can be found, inter alia, on page 5, last line of the second full paragraph. Support for claims directed to nucleic acids comprising a portion at least 15 contiguous nucleotides of a sequence of the invention can be found, inter alia, on page 9, third full paragraph. Support for claims directed to nucleic acids comprising an antisense strand of a nucleic acid of the invention can be found, inter alia, on page 7, lines 6 to 9. Support for claims directed to cells comprising a nucleic acid of the invention, where the cell is a bacterial cell, a fungal cell, a yeast cell, an insect cell, a plant cell or an animal cell, can be found, inter alia, on the paragraph spanning page 13 to page 14, and on the paragraph spanning page 14 to page 15.

Objections to the Claims

The Patent Office objected to claims 29 to 45 for the recitation of "isolated fragment." The Patent Office suggested inserting the term "nucleic acid" or "polynucleotide" before the term "fragment." The instant amendment addresses this issue.

In the Advisory Action, the Patent Office noted that Applicant's proposed amendment would appear to overcome this objection.

Issues under 35 U.S.C. §112, second paragraph

Claims 1 to 9, 13, 14 and 17 to 45 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The term "an alpha-galactosidase activity"

In the Advisory Action, the Patent Office noted that entry of the term "an alpha-galactosidase activity" would result in a rejection under 35 U.S.C. §112, second paragraph, and would require a new search. The instant amendment addresses this issue.

The term "complementary"

The Patent Office maintained the rejection of claims 1 (claims 2-4, 6-9, 13, 14, and 17-23 which depend therefrom) and 5 for allegedly being indefinite in the recitation of "a polynucleotide that is complementary."

The Patent Office is concerned that a skilled artisan may not recognize the scope of the complementary polynucleotides encompassed by the claims. The Patent Office alleges that it is unclear whether Applicants' claimed complementary strand is partial complement (i.e., a fragment) or a complete complement.

The instant amendment to the pending claims addresses this issue for claims 1, 2 to 4, 6 to 9, 13, 14 and 17 to 23.

The Patent Office has suggested use of the term "completely complementary" to clarify whether the claimed complementary strand is a partial (i.e., nucleic acid fragment) or a complete complement. Applicants have addressed this issue in new claims 46 and 47.

In the Advisory Action, the Patent Office noted that Applicant's proposed amendment would appear to overcome this rejection.

The terms "hybridization" and "stringent"

The Patent Office alleges that claims 24 and 32 (claims 40, 41, and 45 which depend therefrom) are indefinite in the recitation of the term "hybridizes" as it is allegedly unclear as to the conditions used for the hybridization. The instant amendment addresses this issue.

The Patent Office alleges that claims 26 and 32 are indefinite in the recitation of the term "stringent conditions" because the specification does not define what conditions constitute "stringent." Applicants' respectfully traverse, noting that the term "stringent conditions" is defined in the specification. However, only to expedite prosecution, claims 26 and 32 are canceled, without prejudice.

In the Advisory Action, the Patent Office noted that the amendment proposed in Applicants' after final amendment (not entered) would not appear to overcome this rejection because the term "comprise" is open-ended claim language. The instant amendment addresses this issue.

The phrase "portion of a polynucleotide"

The Patent Office alleged that claims 29 (claims 35-37 and 42 which depend therefrom), 30, 31 (claims 38, 39, and 44 which depend therefrom), 33, 34 (claims 40, 41, and 45 which depend therefrom) are indefinite for the recitation of "portion of a polynucleotide." One of skill in the art would understand that a "portion" of an article is less than the whole article. Solely to expedite prosecution, Applicants have amended the claims to address this issue.

In the Advisory Action, the Patent Office noted that Applicant's proposed amendment would appear to overcome this rejection.

The phrase "the fragment encodes a polynucleotide"

The Patent Office alleged that claim 29 (claims 35-37 and 42 which depend therefrom) is confusing for the recitation of "the fragment encodes a polynucleotide." Applicants have amended claim 29 to obviate this rejection.

In the Advisory Action, the Patent Office noted that Applicant's proposed amendment would appear to overcome this rejection.

The phrase "capable of identifying a polynucleotide ... "

The Patent Office alleged that claims 31 (claims 38, 39, and 44 which depend therefrom) and 32-34 (claims 40, 41, and 45 which depend therefrom) are unclear in the recitation of "capable of identifying a polynucleotide encoding a polypeptide having alpha galactosidase activity." Applicants respectfully aver that a skilled artisan would understand what is meant by this phrase. Claims 31 and 32 are directed to polynucleotides with defined physical-chemical structures that enable hybridization to polynucleotides encoding alpha galactosidases. However, in order to expedite prosecution, the instant amendment addresses this issue.

In the Advisory Action, the Patent Office noted that Applicant's proposed amendment would appear to overcome this rejection.

Issues under 35 U.S.C. §112, first paragraph

New matter

The Patent Office alleged that in claim 28 the hybridization condition of “wash in fresh 1X SET at -10 degrees Celsius” is new subject matter. Applicants have amended claim 28 to provide for the wash step found on page 6, lines 4-5, of the specification.

In the Advisory Action, the Patent Office noted that Applicant's proposed amendment would appear to overcome this rejection.

Written Description

The rejection of claims 24, 25, and 27-45 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, has been maintained.

Applicants respectfully request that their remarks regarding this issue as set forth in their response of April 17, 2003 (see pages 16 to 19) be incorporated herein in their entirety.

The Advisory Action

In the Advisory Action, the Patent Office set forth reasons why the section 112, first paragraph, written description rejection was maintained.

One reason the Patent Office alleged that the written description rejection was maintained was because it was allegedly unclear as to the particular function of the encoded polypeptide (noting the issue of indefiniteness for the term “an activity”, also discussed above). The instant amendment addresses this issue.

Another reason the Patent Office alleged that the written description rejection was maintained was because it was allegedly unclear as to what the conditions for hybridization were (noting the issue of indefiniteness for the terms “hybridizes” and “comprises”, also discussed above). This instant amendment addresses this issue.

The Patent Office had concerns regarding claims directed to fragments, e.g., in claim 29. This instant amendment addresses this issue.

Another reason the Patent Office alleged that the written description rejection was maintained was because Example 14 of the Revised Written Description Guidelines, discussed

by Applicants in their last response, is not directed to claims reciting hybridization claims, but is instead drawn to a claim reciting a specific sequence identity. However, the Patent Office noted that hybridization language does not preclude a claim from satisfying the written description requirement.

Applicants cited Example 14 of the Revised Written Description Guidelines for concluding that a disclosure meets the requirements of section 112, first paragraph, as providing adequate written description for a claimed invention directed to a genus of polynucleotides or proteins described by structure (an exemplary nucleic acid or polypeptide sequence), a physico-chemical property (e.g., percent sequence identity or specific hybridization conditions) and function (alpha galactosidase activity). Specific hybridization conditions are analogous to percent sequence identities as a physico-chemical property limitation that can satisfy the requirement that the claimed genus be defined by, inter alia, a physico-chemical property.

The Patent Office alleges that Example 14 of the Revised Written Description Guidelines is distinguishable from the claimed invention in that the 95% sequence of identity of SEQ ID NO:3 in Example 14 constitutes a substantial portion of the claims genus, while the broader claims of the instant claimed invention (drawn to 70%, 80% or 90% sequence identity) do not encompass a comparable "substantial" portion of the claimed genus.

However, Applicants respectfully aver that Example 14 of the Revised Written Description Guidelines does not set forth any "95% sequence identity" bright line rule that a genus directed to polynucleotides or proteins having less than 95% sequence identity do not satisfy the written description requirement of section 112, while claims drawn to 95% sequence identity do satisfy the written description requirement of section 112. This interpretation of Example 14 is further evidenced by recently issued claims directed to, e.g., 72.5% sequence identity, as in USPN 6,593,514 (see Exhibit A of this response); 75% sequence identity, as in USPN 6,586,215 (see Exhibit A of this response); 80% sequence identity, as in USPN 6,596,926 (see Exhibit A of this response); 85% sequence identity, as in USPN 6,590,141 and USPN 6,586,179 (see Exhibit A of this response); 86% sequence identity, as in USPN 6,583,337 (see Exhibit A of this response); 90% sequence identity (and "stringent hybridization"), as in USPN 6,541,684 (see Exhibit A of this response, and also Exhibits in Applicants' after final response).

Applicants also refer to recently issued claims directed to genres of polynucleotides based on stringent hybridization to an exemplary nucleic acid, see, e.g., USPN 6,586,179; USPN 6,583,337 and USPN 6,582,950 (see Exhibit A of this response).

As discussed in the last response (the After Final response of April 17, 2003), Applicants respectfully maintain that the instant claimed invention fully complies with the requirements for written description of a genus of nucleic acids as set forth by Federal Circuit case law. When a disclosed function of an enzyme (e.g., an alpha galactosidase) encoded by claimed nucleic acids is sufficiently correlated to a particular, known structure (e.g., exemplary sequences) and a physical (e.g., physico-chemical) property (e.g., sequence identity or stringent hybridization), the claimed sequences are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Accordingly, in view of the instant response and amendment, Applicants respectfully submit that the claimed invention meets the written description requirement under 35 U.S.C. §112, first paragraph.

Enablement

The rejection of claims 24, 25, and 27 to 45 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not reasonably provide enablement for the genus of claimed polynucleotides has been maintained.

Applicants respectfully request that their remarks regarding this issue as set forth in their response of April 17, 2003 (see pages 16 to 19) be incorporated herein in their entirety.

The Advisory Action

In the Advisory Action, the Patent Office set forth reasons why the section 112, first paragraph, enablement rejection was maintained.

One reason the Patent Office alleged that the enablement rejection was maintained was because it was allegedly unclear as to the particular function of the encoded polypeptide (noting the issue of indefiniteness for the term "an activity", also discussed above). The instant amendment addresses this issue.

Another reason the Patent Office alleged that the enablement rejection was maintained was because it was allegedly unclear as to what the conditions for hybridization were (noting the issue of indefiniteness for the terms "hybridizes" and "comprises", also discussed above). This instant amendment addresses this issue.

The Patent Office had concerns regarding claims directed to fragments, e.g., in claim 29. This instant amendment addresses this issue.

Another reason the Patent Office alleged that the enablement rejection was maintained was because of the broad scope of the claims, the lack of guidance and working examples, and the high degree of unpredictability, an undue amount of experimentation would be required to make and use the invention.

Applicants respectfully maintain that it would not have taken undue experimentation to make and use the claimed invention. The difference between impermissible undue experimentation and permissible routine experimentation was discussed in the previously submitted responses dated April 17, 2003, and August 9, 2002. Guidance as to how much experimentation may be needed and still not be "undue" is set forth by the Federal Circuit in, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). The court acknowledged that because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, screening that would be necessary to make additional [antibody] species was not "undue experimentation."

Analogously, practitioners of molecular biology for the instant invention also recognize that many samples may need to be generated and analyzed to make and identify the claimed polynucleotides. The screening protocols were routine and well known in the art. At the time of the invention the state of the art and the level of skill of the person of ordinary skill in the art was very high. The specification set forth specific conditions for determining sequence identity and specific hybridization conditions. Accordingly, one skilled in the art had sufficient guidance by the specification to make and use the claimed polynucleotides without undue experimentation. Thus, the skilled artisan using Applicants' written disclosure could have practiced the claimed invention without undue experimentation.

Regarding working examples, compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. A patent need not teach, and preferably omits, what is well known in the art. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984); see also MPEP §2164.02. As noted above, screening protocols for making the claimed polynucleotides were routine and well known in the art at the time of the invention.

In light of the instant amendment and remarks, Applicants respectfully submit that the specification enables one of ordinary skill in the art to make and use the genus of polynucleotides of the claimed invention.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs. Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050. Please credit any overpayment to this account.

Applicant : Murphy, et al.
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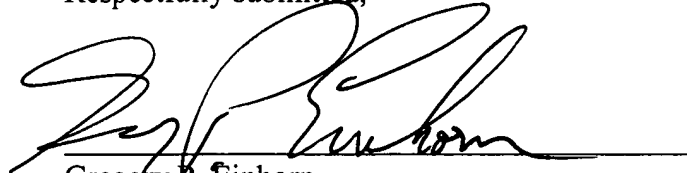
Attorney's Docket No.: 09010-004002

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date:

Aug. 7, 2003



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